MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	**Bioengineered Tissue Products for Wound Treatment and Surgical Interventions**
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Product Disclaimer	• *If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.* • *If a commercial product (including an Essential Plan product) or a Medicaid product covers a specific service, medical policy criteria apply to the benefit.* • *If a Medicare product covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.*

POLICY STATEMENT

I. Based upon our criteria and assessment of the peer-reviewed literature, each of the following bioengineered tissue products has been proven to be medically effective and, therefore, is considered **medically appropriate** for the listed indications, when criteria are met.

Indication	**Biologic tissue product**	**FDA***	**Class**	**Criteria**
Diabetic Foot Ulcers	AlloPatch	Human tissue	Human reticular acellular dermis	1. The patient has adequate arterial blood supply as evidenced by ankle-brachial index (ABI) of 0.65 or greater in the limb being treated; 2. The patient is competent and/or has support system required to participate in follow-up care associated with treatment with a bioengineered tissue product; 3. Ulcers are full thickness, extend through the dermis but without tendon, muscle, capsule or bone exposure, and of greater than three weeks' duration for which standard wound therapy has failed;
	Apligraf	PMA	Cellular, bilayered skin substitute; human-derived composite cultured skin	
	AmnioBand Membrane	Human Tissue	Dehydrated human placental membrane	
	Biovance	Human Tissue	Dehydrated, decellularized human amniotic tissue membrane	
	Dermagraft	PMA	Interactive wound dressing; human-derived composite cultured skin; dermal replacement from neonatal foreskin fibroblasts	

Indication	**Biologic tissue product**	**FDA***	**Class**	**Criteria**
	EpiCord	Human Tissue	Minimally manipulated, lyophilized, non-viable cellular umbilical cord allograft	4. Patient has adequate treatment of underlying disease process(es) contributing to the ulcer; 5. Ulcers are located on foot or toes and are free of infection, redness, drainage, underlying osteomyelitis, surrounding cellulitis, tunnels and tracts, eschar, or any necrotic material that would interfere with adherence of a bioengineered tissue product and wound healing; and 6. Patient's current HbA1C does not exceed 12%.
	EpiFix	Human Tissue	Dehydrated human amnion chorion membrane (dHACM) allograft	
	Grafix CORE	Human Tissue	Cellular matrix from human placental chorionic membrane	
	Grafix PRIME	Human Tissue	Cellular matrix from human placental amniotic membrane	
	Integra	510k	Bovine-derived tendon collagen and glycosaminglycan	
	Integra Dermal Regeneration Matrix (Omnigraft)	PMA	Bilayered, extracellular, cross-linked bovine collagen and chondroitin sulfate **Contraindications:** • Known hypersensitivity to bovine collagen, silicone, or chondroitin materials; • Pregnancy; • Clinically diagnosed infected wounds.	
	Oasis Wound Matrix	510k	Collagen matrix from porcine small intestine submucosa, single layer	
Venous Ulcers	Apligraf	PMA	Cellular, bilayered skin substitute; human-derived composite cultured skin	1. The patient has adequate arterial blood supply as evidenced by ankle-brachial index (ABI) of 0.65 or greater in the limb being treated; 2. The patient is competent and/or has support system required to participate in follow-up care.
	Oasis Wound Matrix	510k	Collagen matrix from porcine small intestine submucosa, single layer	

Indication	**Biologic tissue product**	**FDA***	**Class**	**Criteria**
				associated with treatment with a bioengineered tissue product; 3. Ulcers are partial or full thickness and have failed to respond to conservative measures of at least one month duration that have, at a minimum, included regular dressing changes, debridement of necrotic tissue, and standard therapeutic compression. ("Failure to respond" is defined as increase in size or depth or no change in size or depth with no sign or indication that improvement is likely, such as granulation, epithelialization, or progress toward closing); 4. Patient has adequate treatment of the underlying disease process(es) contributing to the ulcer; and 5. Ulcers are free of infection, redness, drainage, underlying osteomyelitis, surrounding cellulitis, tunnels and tracts, eschar or any necrotic material that would interfere with adherence of a bioengineered tissue product and wound healing.
Breast Reconstruction	Alloderm	Human Tissue	Acellular dermal matrix; allogeneic human derived decellularized skin	1. Breast reconstruction surgery following surgical mastectomy
	AlloMax	Human Tissue	Acellular dermal matrix; allogeneic human derived decellularized skin	
	Cortiva	Human tissue	Acellular dermal matrix; allogeneic human derived decellularized skin	
	DermACELL AWM	Human Tissue	Decellularized regenerative human tissue matrix allograft	
	DermaMatrix	Human Tissue	Human skin allograft	

Indication	**Biologic tissue product**	**FDA***	**Class**	**Criteria**
	FlexHD	Human Tissue	Acellular dermal matrix	
	GraftJacket	Human Tissue	Bilaminate, acellular regenerative tissue; allogeneic, human-derived, decellularized skin	
Nasal Repairs	Alloderm	Human Tissue	Acellular dermal matrix; allogeneic, human-derived, decellularized skin	1. Septal repair, septal perforation repair, reconstructive septorhinoplasty
Non-primary Hernia Repair	Alloderm	Human Tissue	Acellular dermal matrix; allogeneic, human-derived, decellularized skin	1. When chronic infection contraindicates the use of mesh or other conventional repair
Parotidectomy	Alloderm	Human Tissue	Acellular dermal matrix; allogeneic, human-derived, decellularized skin	
Burns	Integra Dermal Regeneration Matrix (Omnigraft)	PMA	Bilayered, extracellular, cross-linked bovine collagen and chondroitin sulfate **Contraindications:** • Known hypersensitivity to bovine collagen, silicone, or chondroitin materials; • Pregnancy; • Clinically diagnosed infected wounds.	1. The patient is competent to understand the need for immobilization and the need for a second surgical procedure for application of an ultra-thin epidermal graft, regular follow-ups, and rehabilitation; 2. Insufficient autograft is available at the time of burn excision; and 3. The burn site is free of residual eschar.
	Biobrane	PMA	Collagen (porcine type 1) incorporated with silicone and nylon	1. The patient is competent to understand the need for immobilization and/or has the support system required to participate in follow-up care associated with treatment with a bioengineered tissue product; 2. The burn is superficial, partial-thickness with limited involvement of the dermis (less than or equal to 25% total body surface area); and 3. The burn is clean, non-infected, and free of nonviable tissue and coagulation eschar.

Indication	**Biologic tissue product**	**FDA***	**Class**	**Criteria**
	Epicel	HDE	Cultured epidermal autograft; combined human and animal dermal cellular material	1. Full thickness burns over greater than 30% of the body; 2. The patient is competent to understand the need for immobilization and the need for a second surgical procedure for application of an ultra-thin epidermal graft, regular follow-ups, and rehabilitation; 3. Insufficient autograft is available at the time of burn excision; and 4. The burn site is free of residual eschar.

*PMA U.S. Food and Drug Administration (FDA) pre-market approval process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices

*510(k) - Premarket submission made to FDA to demonstrate that the device to be marketed is at least as safe and effective (i.e., substantially equivalent) to a legally marketed device that is not subject to PMA

*Human tissue - Donated, banked human skin regulated by the American Association of Tissue Banks and FDA guidelines

II. Based upon our criteria and assessment of the peer-reviewed literature, all other bioengineered tissue products including but not limited to, those listed below, have not been medically proven to be effective and, therefore, are considered **investigational** or uproven for ANY indication:

Biologic tissue product	**Class**
ACell UBM Hydrated/Lyophilized Wound Dressing	Porcine collagen
Affinity	Human amniotic tissue membrane
Allogen, Allogen Liquid	Human liquid amnion
AlloSkin	Epidermal and dermal allograft
AlloSkin RT	Epidermal and dermal allograft
AlloSource	Cryopreserved human cadaver skin
AlloWrap DS or Dry	Human amniotic tissue membrane
AmnioAMP-MP	Decellularized dehydrated human amniotic membrane
AmnioArmor	Dehydrated human amniotic membrane allograft
AmnioCare	
AmnioCore	Dehydrated, non-viable cellular amniotic membrane
AmnioCyte Plus	Human amniotic membrane
AmnioExcel	Human amniotic tissue membrane
AmnioFix	Human amniotic membrane
AmnioGenix	
AmnioHeal amniotic membrane	Amniotic membrane graft
AmnioMatrix	Human amniotic tissue membrane
Amnio-Maxx or Amnio-Maxx Lite	Dehydrated human amniotic tissue membrane
AmnioMTM	Cryopreserved amnion allograft
AMNIOREPAIR or AltiPly	Lyophilized placental membrane
AmnioShield	

Biologic tissue product	**Class**
AmnioStrip	
AmnioText or AmnioText Patch	Amniotic membrane derived, human tissue allograft
Amniotic fluid injection	
Amniowrap	Amniotic/chorionic tissue allograft
Amniply	Amniotic membrane graft
Aongen Collagen Matrix	
Architect ECM, PX, FX	
Ascent	Dehydrated cell and protein concentrate (dCPC) injectable derived from human amniotic fluid
Artacent AC	
Artacent Cord	Umbilical cord allograft
Artacent Wound	
ArthroFlex (aka FlexGraft)	Decellularized human allograft dermis
Atlas Wound Matrix	
Avagen Wound Dressing	
Avaulta Plus	Porcine-derived polypropylene composite
AxoBioMembrane, Amnion Bio	Dehydrated human amniotic membrane allograft
AxoGuard Nerve Protector (AxoGen)	
Axolotl Ambient	Human amniotic flowable allograft
Axolotl Cryo	Human amniotic flowable allograft
Axolotl DualGraft	Human amniotic allograft, decellularized, dehydrated placental membrane
Axolotl Graft	Human amniotic allograft, decellularized, dehydrated placental membrane
BellaCell HD	Human acellular dehydrated dermis regenerative tissue matrix
BioDexcel	
BioDFence/ BioDfactor	Human amniotic tissue membrane
BioDmatrix	
BioDrestore Elemental Tissue Matrix	
BioNextPATCH	Dehydrated amniotic membrane allograft
Biotape reinforcement matrix	
BioWound, Plus, XPlus	Human amnion based membranes
carePATCH	Dehydrated amniotic membrane allograft
Cellesta	
Cellesta Cord	Umbilical cord allograft product
Cellesta Flowable Amnion	
CellerateRX	
Clarix 100	
Clarix Cord 1K	
Clarix Flo	Human amniotic tissue and umbilical cord membrane
Cogenex amniotic membrane or flowable amnion	Amniotic membrane allograft
CollaFix	
CollaCare	
Collamend	Porcine derived decellularized collagen
CollaWound	
Coll-e-derm	
Collexa	

Biologic tissue product	**Class**
Colleiva	
Conexa	Porcine dermis tissue substitute
Corecyte	Wharton's jelly-derived human cell and tissue product
Coretext	Wharton's jelly-derived human tissue allograft
CorMatrix	Acellular matrix composed of porcine small intestine submucosa
Corplex	Human umbilical cord allograft
Corplex P	Wharton's jelly allograft
CRXa	
Cryo-Cord	Cryopreserved semi-transparent, collagenous membrane allograft
Cygnus Solo	
Cygnus Matrix	
Cygnus Max	
Cymetra	Allogeneic, cadaver-derived, decellularized skin; micronized particulate form of AlloDerm
Cytal Burn Matrix	Porcine collagen wound dressing
Cytal Wound Matrix	Porcine collagen wound dressing
Dehydrated human amniotic membrane allograft (AmnioPro, BioFix, FlowerPatch)	
Dermacyte Amniotic Membrane Allograft	Amniotic membrane allograft
Derma-Gide	
DermaPure	Single-layer, decellularized, dermal allograft
DermaSpan	Acellular dermal matrix
Dermavest	Human placental connective tissue matrix
Derm-Maxx	Freeze dried decellularized dermal matrix allograft
DryFlex	Human amnion allograft
Durepair Regeneration Matrix	
Endoform Dermal Template	Ovine-derived extracellular matrix
ENDURAgen	Porcine dermal acellular collagen matrix
EpiFix Injectable	
Excellagen	Bovine collagen gel
E-Z Derm	Porcine-derived, decellularized fetal skin
FlexiGraft	
FloGraft	
Fluid Flow, Fluid GF	Human amniotic flowable allografts
Fortaderm (see PuraPly)	
Fortiva Porcine Dermis	
GammaGraft	Irradiated, human skin composite allograft
Genesis amniotic membrane	
Glyaderm	Glycerol-preserved, acellular human dermis
GraftJacket Xpress	Micronized, decellularized soft tissue scaffold
Graftskin (see Apligraf)	
Guardian	Dehydrated human placental membrane
hMatrix	Acellular dermal matrix
Hyalomatrix	Hyaff 11 (hyaluronic acid) and silicone
Hyalomatrix PA	

Biologic tissue product	**Class**
HydroFix	
Integra Bilayer Wound Matrix	Bovine-tendon collagen, glucoseaminoglycan, and silicone
Integra Flowable Wound	Granulated, cross-linked, bovine tendon collagen and glycosaminoglycan
InteguPly	Acellular dermal matrix
Interfyl	
Kerecis Omega 3	Fish skin xenograft
Keroxx	
Laserskin (see Hyalomatrix)	
MariGen/ Alphaplex with MariGen Omega3	Cod fish skin
MatriDerm	
Matrion	
Matristem Burn Matrix (see Cytal Burn Matrix)	
Matristem Wound Matrix (see Cytal Wound Matrix)	
Matrix HD	
MediHoney	
Mediskin	Porcine-derived, decellularized fetal skin, frozen
Membrane Graft	Human amniotic allograft membrane
Membrane Wrap	Human amniotic allograft membrane
MemoDerm	
Miroderm	
MyOwn Skin	Autologous, homologous human skin product
Neopatch	Dehydrated human placental membrane tissue
Neox	Human amniotic and umbilical cord tissue membrane
Neox 1K	Human amniotic tissue membrane
Neox Flo	Human amniotic tissue and umbilical cord membrane
Neox Wound Matrix	
Novachor	
NovaFix or NovaFix DL	Dehydrated human amniotic membrane allograft
Nudyn	Acellular, flowable allograft tissue matrix derived from donated human amniotic membrane
NuShield	Dehydrated human placental membrane
OASIS Burn Matrix	Extracellular matrix from porcine small intestine submucosa, bi-layered
OASIS Ultra	Collagen matrix from porcine small intestine submucosa, tri-layered
Orcel	Composite skin substitute; human-derived, composite cultured skin; bilayered cellular matrix
Orthoadapt	Equine-derived decellularized collagen
PalinGen Membrane, Hydromembrane	
PalinGen Flow, SportFlow	
Pelvicol	Porcine-derived decellularized collagen
Pelvisoft	Porcine-derived decellularized collagen
Permacol	Acellular, porcine, dermal collagen and elastin xenograft
PolyCyte	Wharton's jelly-derived human cell and tissue product
PriMatrix	Acellular, collagen dermal tissue matrix; fetal bovine-derived, decellularized skin product

Biologic tissue product	**Class**
PriMatrix Dermal Repair Scaffold	
Procenta	Acellular, sterile, human placental-derived allograft
ProgenaMatrix	Human keratin matrix derived from human hair
Prolifix	
Protext	Wharton's jelly-derived human tissue allograft
PuraPly Antimicrobial & PuraPly Wound Matrix (previously Fortaderm)	Fenestrated porcine allograft
RegenePro	
REGUaRD	Acellular (human) dermal allograft matrix derived from donated allograft placental membrane tissue
Repliform	Acellular human dermis
Repriza	Acellular dermal matrix
Restore	Porcine small intestine submucosa
Restorigin	Amniotic tissue matrix
Revitalon (previously Amnioclear)	Human amniotic tissue membrane
SkinTE	Autologous, homologous, full–thickness skin product
StrataGraft	NIKS cells, tissue keratinocytes
Strattice	Porcine dermis xenographic tissue
Stravix, Stravix PL	Cryopreserved human placental tissue composed of umbilical amnion and Wharton's jelly
Suprathel	Fully synthetic dressing
SureDerm	Human acellular dermal matrix
Surfactor	Acellular, flowable allograft tissue matrix derived from donated human amniotic membrane
SurgiCORD	Umbilical tissue membrane allograft
SurgiGRAFT-DUAL	Minimally processed bilayer allograft
Surgigraft	
SurGraft	Dehydrated amniotic membrane sheet
SurgiMend	Acellular dermal tissue matrix from fetal bovine dermis
Talymed	
TenoGlide	
TenSIX	Acellular dermal matrix
TheraSkin	Cryopreserved, allogeneic human skin
Therion	Dehydrated human placental membrane tissue
Tissuemend	Bovine-derived, decellularized skin product
TranZgraft	Acellular dermal matrix
TruSkin	
Veritas Collagen Matrix	Non-cross-linked bovine pericardium
Woundfix, Woundfix Plus, Woundfix Xplus	Human amnion-based membranes
XCellerate	Lyophilized amniotic membrane allograft
XCM Biologic	Porcine dermal matrix
XenMatrix AB	
Xwrap	

Refer to Corporate Medical Policy #1.01.38 Negative Pressure Wound Therapy (Vacuum Assisted Closure).

Refer to Corporate Medical Policy #2.01.24 Growth Factors for Wound Healing and Other Conditions.

Refer to Corporate Medical Policy #10.01.01 Breast Reconstruction Surgery.

Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services.

This policy does not address fibrin sealants (e.g., Tisseel).

This policy does not address the use of amniotic membrane products for repair of ocular defects.

POLICY GUIDELINES

I. Utilization of specific products are medically appropriate only when used in accordance with FDA product approval and when the above policy criteria are met.

II. If a wound has not responded to standard of care by achieving a 50% or better wound reduction after four weeks of standard of care, a single application of a bioengineered tissue product was thought to be all that was required to affect wound healing in wounds likely to be improved by this treatment. Based on clinical input from wound specialists, refractory wounds rarely heal with one graft application and may require additional graft applications, no more frequently than once per week, until the wound heals. Re-application of a product is appropriate only if there has been measurable response to the first application. Re-application less than one year after successful treatment is considered treatment failure and **not medically appropriate**.

III. Treatment of venous stasis ulcers that extend above the malleoli is beyond the scope of practice of podiatrists.

DESCRIPTION

Bioengineered tissue products are cellular (contain living cells) or acellular (no biological component) matrices that can be derived from human tissue (autologous or allogeneic), nonhuman tissue (xenographic), synthetic materials, or a composite of these materials. Manufacturing processes vary, but generally involve seeding selected cells onto a matrix, where they receive proteins and growth factors necessary for them to develop into the desired tissue. The tissue may then be used for a variety of procedures, including breast reconstruction, treatment of severe burns, and healing of diabetic and venous ulcers.

RATIONALE

Bioengineered skin and soft tissue substitutes are being investigated for a variety of conditions. Overall, the number of bioengineered skin and soft tissue substitutes is large, but the evidence is limited for any specific product. Relatively few products have been compared with the standard of care (SOC), and then only for some indications. Most trials identified were industry-sponsored and open label, with no masking indicating potential performance bias. The data on many of the industry-sponsored trials had incomplete outcome data, indicating attrition bias. Additional studies with larger numbers of subjects are needed, to evaluate the effect of bio-engineered skin and soft tissue substitutes versus the current SOC or current advanced wound therapies (i.e., Apligraf or Dermagraft). Overall, results of these studies do not provide convincing evidence that many of these products are more effective than SOC or current advanced wound therapies for healing diabetic foot or venous ulcers. Additional trials with a larger number of subjects are needed, to determine whether these products improve health outcomes.

In December 2012, the Agency for Health Research and Quality (AHRQ) completed a technology assessment addressing *Skin Substitutes for Treating Chronic Wounds.* The assessment addresses 57 products currently available in the U.S. that are used to manage or treat chronic wounds and are regulated by FDA. Based on FDA regulations, skin substitutes can be organized into four groups: human-derived products regulated as HCT/Ps (human cells, tissues, and tissue-based products), human- and human/animal-derived products regulated through PMA or humanitarian device exemption (HDE), animal-derived products regulated under the 510(k) process, and synthetic products regulated under the 510(k) process. One of the report's goals was to begin to characterize the state of the evidence on skin substitutes as wound care products for chronic wounds. Eighteen randomized, controlled trials (RCTs) examining only seven of the skin substitute products identified for the report met the inclusion criteria. The author's evaluation of the clinical literature indicates that studies comparing the efficacy of skin substitutes to alternative wound care approaches are limited in number, apply mainly to

generally healthy patients, and examine only a small portion of the skin substitute products available in the United States. The results of the available studies cannot be extended to other skin substitute products because of differences in active components in the various products. The studies available were not generalizable to the broader patient populations that are not as healthy as the patients in the studies. Also missing from the evidence base were studies that compared the various types of skin substitute products. Only two of the 18 studies compared two skin substitute products. How a human dermal substitute compares with a human derived skin substitute, when treating a diabetic foot ulcer or a vascular leg ulcer, is unknown. Such comparisons could be useful to clinicians trying to decide which wound treatment products to use. Additional studies in the area of wound care would be helpful, to provide treatment data for many of the other skin substitute products, to allow better comparisons between wound care products, and to provide better information on wound recurrence when using skin substitute products.

Product Categories:

Acellular Dermal Matrices (ADM):

There is a small amount of evidence utilizing acellular dermal matrix products in breast reconstruction that does not show any difference in outcomes among the different types of ADM products.

A retrospective review compared complication rates following breast reconstruction with AlloDerm or FlexHD in 382 consecutive women (547 breasts). A total of 81% of the patients underwent immediate reconstructions; 165 used AlloDerm, and 97 used FlexHD. Mean follow-up was 6.4 months. Compared with breast reconstruction without use of AlloDerm or FlexHD, ADM had a higher rate of delayed healing (20.2% vs 10.3%), although this finding might be related to differences in fill volumes. In univariate analysis, there were no significant differences in complications (return to the operating room, surgical site infection, seroma, hematoma, delayed healing, or implant loss) between AlloDerm and FlexHD. In multivariate analysis, there were no significant differences between AlloDerm and FlexHD for the return to the operating room, surgical site infection, seroma, or delayed healing. Independent risk factors for implant loss included the use of FlexHD, single-stage reconstruction, and smoking. (Liu et al., 2014).

Another retrospective review published in 2013 compared complication rates following use of AlloDerm (n=136) or FlexHD (n=233) in a consecutive series of 255 patients (369 breasts). Total complication rates for the two products were similar (19.1% for AlloDerm and 19.3% for FlexHD). Analysis by type of complication showed no significant difference between the products, and regression analysis controlling for differences in baseline measures found that the type of ADM was not a risk factor for any complication (Seth et al., 2013).

A retrospective review of complication rates when AlloDerm (n=49), DermaMatrix (n=110), or FlexHD (n=62) was used for tissue expander breast reconstruction was published in 2012. Clinically significant complications were defined as cellulitis, abscess, seroma, expander leak or puncture, skin necrosis, wound dehiscence, or hematoma. The total clinically significant complication rate was 22% with AlloDerm, 15% with DermaMatrix, and 16% with FlexHD (not significantly different). Infectious complication rates for the three products were the same at 10%. When compared with breast reconstruction without an ADM (n=64), there was no significant difference in the total complication rate (17% vs 11%), but there was a trend toward a higher incidence of infectious complications (10% vs 2%, p=0.09) (Brooke et al., 2012).

Amniotic Tissue Membrane:

Human amniotic membrane is classified by the FDA as banked human tissue and, therefore, does not require FDA approval. Examples of amniotic tissue membrane include, but are not limited to, EpiFix and Grafix. Results from small studies are encouraging, but preliminary. Further large, randomized, controlled studies are needed before conclusions may be reached regarding the efficacy of these products.

A review article, published in 2015 by Zelen et al., addresses the use of human amnion/chorion membrane (dHACM) for lower extremity repair. The article states:

> Although there are limited data available regarding most amniotic membrane-based products, there is substantial preclinical and clinical evidence supporting the rationale and effectiveness of dHACM allograft as a

treatment modality. The rapidly growing body of evidence suggests that the properties inherent in dHACM promote tissue regeneration and healing, recruiting patients' own stem cells into the wounded area. Randomized controlled trials evaluating dHACM now include more than 200 patients collectively and the results consistently show improved healing. Use of dHACM has been shown to be more clinically effective and cost-effective than other frequently used advanced wound care products. This cost-effectiveness results from dHACM showing higher healing rates and more rapid healing than other advanced wound care products. Cost-effectiveness is also enhanced through the availability of grafts of multiple sizes, which reduces wastage, and through ease of handling and storage for clinical use. Ongoing and future studies will further define and establish the value of amniotic membrane for chronic tissue repair and regeneration.

A small, industry-sponsored, non-blinded, RCT comparing the use of EpiFix (n=13) with SOC (moist wound therapy, n=12) for diabetic foot ulcers of at least four weeks' duration was published in 2013. EpiFix was applied every two weeks if the wound had not healed, with weekly dressing changes consisting of non-adherent dressing, moisture retentive dressing, and a compression dressing. Standard moist wound dressing was changed daily. After four weeks of treatment, EpiFix-treated wounds had reduced in size by a mean of 97.1%, compared with 32.0% for the SOC group. Healing rate (complete epithelialization of the open area of the wound) was 77% for EpiFix, compared with 0% for SOC. After six weeks of treatment, wounds were reduced by 98.4% with EpiFix treatment, compared with -1.8% for SOC. The healing rate was 92% with EpiFix, compared with 8% with standard treatment alone (Zelen et al., 2013).

Treatment with EpiFix, Apligraf, or standard wound care was compared in a multicenter randomized, controlled study. Sixty patients with chronic lower extremity diabetic ulcers were randomized to treatment with Epifix (dehydrated human amniotic membrane), Apligraf (human skin allograft with living fibroblasts and keratinocytes), or standard wound care. Although the patient and site investigator could not be blinded due to differences in products, wound healing was verified by three independent physicians who evaluated photographic images. The median wound size was 2.0 cm^2 (range, 1.0-9.0), and the median duration of the index ulcer was 11 weeks (range, 5-54). After six weekly treatments, the mean percent wound area healed was 97.1% for EpiFix, 80.9% for Apligraf, and 27.7% for standard care; 95% of wounds had healed in the EpiFix group compared with 45% treated with Apligraf and 35% who received standard wound care ($p<0.003$). The estimated median time to wound closure, based on Kaplan-Meier analysis, was 13 days for EpiFix, compared with 49 days for both Apligraf and SOC ($p<0.001$). Based on the updated Zelen et al. (2015) article, data were included on treatment of 226 diabetic foot ulcers from 99 wound care centers. Although wounds for the two groups were compared at baseline, the rationale for using a particular product was not reported. There were 163 wounds treated with Apligraf and 63 treated with Epifix. By week 24, 72% of the wounds treated with Apligraf and 47% of the wounds treated with Epifix had closed. The median time to closure was 13.3 weeks for Apligraf and 26.0 weeks for Epifix.

In 2015, Kirsner et al. reported an industry-sponsored observational study comparing the effectiveness of Apligraf and EpiFix in a real-world setting. Data were obtained from a wound care–specific database from 3000 wound care facilities. The database included 1458 diabetic ulcers treated for the first time in 2014 with Apligraf (n=994) or EpiFix (n=464). Using the same criteria as the 2015 study by Zelen (described above), data were included on the treatment of 226 diabetic foot ulcers from 99 wound care centers. Foot wounds were included with size between 1 cm2 and 25 cm2, duration of one year or less, and wound reduction of 20% or less in the 14 days prior to treatment. Although wounds for the two groups were comparable at baseline, the rationale for using a particular product was not reported. There were 163 wounds treated with Apligraf (mean, 2.5 applications) and 63 treated with EpiFix (mean, 3.5 applications, $p=0.003$). By week 24, 72% of wounds treated with Apligraf and 47% of wounds treated with EpiFix had closed ($p=0.01$).

Treatment with Grafix or standard wound care was compared in a small, multi-centered RCT for diabetic foot ulcers (Lavery et al., 2014). Although the results were positive, the sample size was small, with 50 treated with Grafix and 47 in the control group treated with SOC. The primary end point was complete wound closure by 12 weeks. Grafix patients who achieved full closure was 62% versus 21% in the control group receiving SOC. Ananian et al. (2018) reported a prospective, randomized, single-blind study comparing the efficacy of Grafix with Dermagraft. The end result of this study was measured by wound closure and showed that Grafix (48.4% closure) is non-inferior to Dermagraft (38.7% closure).

AmnioBand was compared to SOC for treatment of non-healing diabetic foot ulcers in an industry-sponsored, multi-center study (DiDomenico et al., 2016). Forty patients were randomized to SOC or SOC with AmnioBand for up to 12 weeks. Complete healing by six weeks was observed for 70% of wounds treated with SOC and AmnioBand versus 15% treated with SOC alone. At 12 weeks, complete healing was observed in 85% of the SOC and AmnioBand group versus 25% treated with SOC alone. Limitations of the study were small sample size, a drop-out rate of 9/40, and the wound area in the control group was larger than in the treatment group.

The limited published, peer-reviewed, medical literature does not provide sufficient information to determine that the use of Biovance has a definite, positive effect on health outcomes in treating lower extremity diabetic ulcers.

Other Products:

AlloDerm is classified by the FDA as human tissue and is approved for use in burns and full-thickness wounds. There is limited scientific evidence in the form of retrospective case series to support the use of AlloDerm in rare cases of non-primary hernia repair when chronic infection contraindicates the use of mesh or other conventional repair.

Although the literature investigating the use of AlloDerm in breast reconstruction surgery consists of small case series that lack long-term data on effectiveness and safety, they all reach favorable conclusions. The use of AlloDerm obviates many of the current disadvantages to implant breast reconstruction, including thinning of the muscle layer causing visible rippling and contour irregularities. In the multi-step processing of AlloDerm, the epidermis and all of the dermal cellular components are removed, leaving no reservoir for viral agents. As a result, no immune response is elicited after placement of the allograft.

Literature regarding the use of AlloDerm in parotidectomy also consists of small case series; however, the studies support that AlloDerm is beneficial in preventing Frey's syndrome after parotidectomy.

AlloPatch, which is a pliable human reticular, acellular dermis, was compared to SOC in a 2016 industry-sponsored, multicenter trial by Zelen et al. The trial was powered to detect a 45% difference between groups in percentage healing at six weeks with 20 patients per group. Evaluation of the outcome measures was not blinded. At six weeks, 65% (13/20) of wounds treated with AlloPatch had healed, compared to 5% (1/20) in the SOC-alone group ($p<0.001$). After adjusting for wound area at baseline, the hazard ratio for healing was 168 (95% CI, 10 to 2704; $p<0.001$), indicating a lack of precision in the estimate. Per protocol, 10 patients in the SOC group and one in the AlloPatch group exited the study at six weeks because their wounds failed to reduce in area by at least 50%. According to intent-to-treat (ITT) analysis with last observation carried forward, the percentage of wounds healed at 12 weeks was 80% in the AlloPatch group, compared to 20% in the SOC group. However, because there was a high (50%) withdrawal rate in the SOC group, this result has a high risk of bias.

Biobrane was granted pre-market approval by the FDA as a temporary covering of full-thickness burns until autografting is clinically appropriate.

The Integra Dermal Regeneration Template (Integra) was granted pre-market approval by the FDA for use in post-excisional treatment of life-threatening, full-thickness or deep partial-thickness thermal injuries where sufficient autograft in not available at the time of excision or not desirable due to the physiological condition of the patient, and for the repair of scar contractures when other therapies have failed or when donor sites for repair are not sufficient or desirable due to the physiologic condition of the patient. Evidence for use of the Integra for contracture release procedures consists only of a retrospective case series without controls.

In January 2016, the FDA approved the Integra Dermal Regeneration Template, marketed as Omnigraft, for use in the treatment of partial- and full-thickness neuropathic diabetic foot ulcers that are greater than six weeks in duration, with no capsule, tendon, or bone exposed, when used in conjunction with standard diabetic ulcer care. Randomized, controlled studies have been shown to improve healing of chronic, non-healing diabetic foot ulcers with the use of Omnigraft. The Foot Ulcer New Dermal Replacement (FOUNDER) multicenter study on the use of Integra Dermal Regeneration Template for chronic, non-healing diabetic foot ulcers was conducted under an FDA-regulated investigational device exemption. A total of 307 patients with at least one chronic diabetic foot ulcer were randomized to treatment with the Integra Template or a control condition (0.9% sodium chloride gel). Treatment was given for 16 weeks or until wound

closure. There was a modest increase in wound closure with the Integra Template (51% vs 32%) and a shorter median time to closure (43 days versus 78 days). There was a strong correlation between investigator-assessed and computerized planimetry assessment of wound healing (*r*=0.97). Kaplan-Meier analysis showed the greatest difference between groups in wound closure up to 10 weeks, with diminishing differences after 10 ~~0~~ weeks. Strengths of the study included adequate power to detect an increase in wound healing of 18%, which was considered to be clinically significant, as well as secondary outcomes of wound closure and time to wound closure by computerized planimetry and intention-to-treat (ITT) analysis. (Driver et. al., 2015)

The Oasis Wound Matrix, Oasis Burn Matrix, and Oasis Ultra Tri-Layer Matrix have FDA 510(k) approval in the management of wounds, including partial- and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic vascular ulcers, tunneled undermined wounds, surgical wounds, trauma wounds, and draining wounds. The Oasis Wound Matrix (Cook Biotech) is a xenogeneic collagen scaffold derived from porcine small intestinal mucosa. Niezgoda, et al. (2005) compared healing rates at 12 weeks for full-thickness diabetic foot ulcers treated with the OASIS Wound Matrix (an acellular wound care product) to Regranex Gel. This industry-sponsored, multicenter RCT was conducted at nine outpatient wound care clinics and involved 73 patients with at least one diabetic foot ulcer. Patients were randomized to receive either Oasis Wound Matrix (n=37) or Regranex Gel (n=36) and a secondary dressing. Wounds were cleansed and debrided, if needed, at a weekly visit. The maximum treatment period for each patient was 12 weeks. After 12 weeks, 18 (49%) Oasis-treated patients had complete wound closure, compared with 10 (28%) Regranex-treated patients. Oasis treatment met the noninferiority margin, but the study did not demonstrate that healing in the Oasis group was statistically superior (p=0.055). Post hoc subgroup analysis showed no significant difference in incidence of healing in patients with type 1 diabetes (33% vs 25%) but showed a significant improvement in patients with type 2 diabetes (63% vs 29%). There was also an increased healing of plantar ulcers in the Oasis group (52% vs 14%).

PriMatrix received FDA 510(k) approval in 2006 for the management of wounds that include: partial- and full-thickness wounds; pressure, diabetic, and venous ulcers; second-degree burns; surgical wounds, including donor sites/grafts, post-Mohs surgery, post-laser surgery, and podiatric, wound dehiscence; trauma wounds, including abrasions, lacerations, and skin tears; tunneled/undermined wounds; and draining wounds.

Theraskin was reported in a small (n=23), industry-funded, randomized comparison of TheraSkin (human skin allograft with living fibroblasts and keratinocytes) to Dermagraft (human-derived fibroblasts cultured on mesh) for diabetic foot ulcers. Wound size at baseline ranged from 0.5 to 18.02 cm^2; the average wound size was about 5 cm^2 and was similar for the two groups (p=0.51). Grafts were applied according to the manufacturer's instructions over the first 12 weeks of the study until healing, with an average of 4.4 TheraSkin grafts (every two weeks) compared with 8.9 Dermagraft applications (every week). At week 12, complete wound healing was observed in 63.6% of ulcers treated with TheraSkin and 33.3% of ulcers treated with Dermagraft (p<0.049). At 20 weeks, complete wound healing was observed in 90.9% of the TheraSkin-treated ulcers, compared with 66.67% of the Dermagraft group (p=0.428). (Sanders et al., 2014). Further large, randomized, controlled studies are needed before conclusions may be reached regarding the efficacy of Theraskin.

CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- *CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.*
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*
- *Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).*

CPT Codes

Code	Description
15271	Application of skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area

Code	Description
15272	each additional 25 sq cm wound surface area, or part thereof
15273	Application of skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
15274	each additional 100 sq cm wound surface area, or part thereof, or each additional 1% body area of infants and children, or part thereof
15275	Application of skin substitute graft to face, scalp, eyelids, mouth, neck ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
15276	each additional 25 sq cm wound surface area, or part thereof
15277	Application of skin substitute graft to face, scalp, eyelids, mouth, neck ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
15278	each additional 100 sq cm wound surface area, or part thereof, or each additional 1% body area of infants and children, or part thereof
15777	Implantation of biologic implant (eg, acellular dermal matrix) for soft tissue reinforcement (ie, breast, trunk)

HCPCS Codes

Code	Description
A2001 **(E/I)**	Innovamatrix ac, per square centimeter *(effective 01/01/22)*
A2002 **(E/I)**	Mirragen advanced wound matrix, per square centimeter *(effective 01/01/22)*
A2003 **(E/I)**	Bio-connekt wound matrix, per square centimeter *(effective 01/01/22)*
A2004 **(E/I)**	Xcellistem, per square centimeter *(effective 01/01/22)*
A2005 **(E/I)**	Microlyte matrix, per square centimeter *(effective 01/01/22)*
A2007 **(E/I)**	Restrata, per square centimeter *(effective 01/01/22)*
A2008 **(E/I)**	Theragenesis, per square centimeter *(effective 01/01/22)*
A2009 **(E/I)**	Symphony, per square centimeter *(effective 01/01/22)*
A2010 **(E/I)**	Apis, per square centimeter *(effective 01/01/22)*
A2014 **(E/I)**	Omeza collagen matrix, per 100 mg *(effective 10/01/22)*
A2015 **(E/I)**	Phoenix wound matrix, per square centimeter *(effective 10/01/22)*
A2016 **(E/I)**	Permeaderm b, per square centimeter *(effective 10/01/22)*
A2017 **(E/I)**	Permeaderm glove, each *(effective 10/01/22)*
A2018 **(E/I)**	Permeaderm c, per square centimeter *(effective 10/01/22)*
A6460 **(E/I)**	Synthetic resorbable wound dressing, sterile, pad size 16 sq. in. or less, without adhesive border, each dressing (e.g. Restrata)
A6461 **(E/I)**	Synthetic resorbable wound dressing, sterile, pad size more than 16 sq. in. but less than or equal to 48 sq. in., without adhesive border, each dressing (e.g. Restrata)
C1849 **(E/I)**	Skin substitute, synthetic, resorbable, per square centimeter *(effective 7/1/20)*

Code	Description
C5271	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
C5272	each additional 25 sq cm or less wound surface area, or part thereof (list separately in addition to code for primary procedure)
C5273	Application of low cost skin substitute graft to trunk, arms, legs, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
C5274	each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof (list separately in addition to code for primary procedure)
C5275	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area up to 100 sq cm; first 25 sq cm or less wound surface area
C5276	each additional 25 sq cm or less wound surface area, or part thereof (list separately in addition to code for primary procedure)
C5277	Application of low cost skin substitute graft to face, scalp, eyelids, mouth, neck, ears, orbits, genitalia, hands, feet, and/or multiple digits, total wound surface area greater than or equal to 100 sq cm; first 100 sq cm wound surface area, or 1% of body area of infants and children
C5278	each additional 100 sq cm wound surface area, or part thereof, or each additional 1% of body area of infants and children, or part thereof (list separately in addition to code for primary procedure)
C9354 **(E/I)**	Acellular pericardial tissue matrix of non-human origin (Veritas), per square cm
C9356 **(E/I)**	Tendon, porous matrix of cross-linked collagen and glycosaminoglycan matrix (TenoGlide Tendon Protector Sheet), per square cm
C9358 **(E/I)**	Dermal substitute, native, non-denatured collagen, fetal bovine origin (SurgiMend Collagen Matrix), per 0.5 square cms
C9360 **(E/I)**	Dermal substitute, native, non-denatured collagen, neonatal bovine origin (SurgiMend Collagen Matrix), per 0.5 square cms
C9363 **(E/I)**	Skin substitute (Integra Meshed Bilayer Wound Matrix), per square cm
C9364 **(E/I)**	Porcine implant, Permacol, per square cm
Q4100	Skin substitute, not otherwise specified
Q4101	Apligraf, per square cm
Q4102	Oasis wound matrix, per square cm
Q4103 **(E/I)**	Oasis burn matrix, per square cm
Q4104 **(E/I)**	Integra bilayer matrix wound dressing (BMWD), per square cm
Q4105	Integra dermal regeneration template (DRT) or Integra Omnigraft dermal regeneration matrix, per square cm
Q4106	Dermagraft, per square cm
Q4107	GRAFTJACKET, per square cm
Q4108	Integra matrix, per square cm

Code	Description
Q4110 **(E/I)**	PriMatrix, per square cm
Q4111 **(E/I)**	GammaGraft, per square cm
Q4112 **(E/I)**	Cymetra, injectable, 1 cc
Q4113 **(E/I)**	GRAFTJACKET XPRESS, injectable, 1 cc
Q4114 **(E/I)**	Integra flowable wound matrix, injectable, 1 cc
Q4115 **(E/I)**	AlloSkin, per square cm
Q4116	AlloDerm, per square cm
Q4117 **(E/I)**	HYALOMATRIX, per square cm
Q4118 **(E/I)**	MatriStem micromatrix, 1 mg
Q4121 **(E/I)**	TheraSkin, per square cm
Q4122	DermACELL, DermACELL AWM or DermACELL AWM Porous, per sq cm
Q4123 **(E/I)**	AlloSkin RT, per square cm
Q4124 **(E/I)**	OASIS ultra tri-layer wound matrix, per square cm
Q4125 **(E/I)**	Arthroflex, per square cm
Q4126 **(E/I)**	MemoDerm, dermaspan, tranzgraft or integuply, per square cm
Q4127 **(E/I)**	Talymed, per square cm
Q4128	FlexHD, AllopatchHD, or Matrix HD, per square cm
Q4130 **(E/I)**	Strattice TM, per square cm
Q4132	Grafix Core and GrafixPL Core, per square cm
Q4133	Grafix PRIME, GrafixPL PRIME, Stravix and StravixPL, per sq cm
Q4134 **(E/I)**	Hmatrix, per square cm
Q4135 **(E/I)**	Mediskin, per square cm
Q4136 **(E/I)**	Ez-derm, per square cm
Q4137 **(E/I)**	AmnioExcel, AmnioExcel Plus or BioDExcel, per sq cm
Q4138 **(E/I)**	BioDFence DryFlex, per sq cm
Q4139 **(E/I)**	AmnioMatrix or BioDMatrix, injectable, 1 cc
Q4140 **(E/I)**	BioDFence, per sq cm
Q4141 **(E/I)**	Alloskin ac, per square cm
Q4142 **(E/I)**	XCM biologic tissue matrix, per square cm
Q4143 **(E/I)**	Repriza, per square cm
Q4145 **(E/I)**	Epifix, injectable, 1 mg
Q4146 **(E/I)**	Tensix, per square cm
Q4147 **(E/I)**	Architect, architect PX, or architect FX, extracellular matrix, per square cm
Q4148 **(E/I)**	Neox Cord 1K, Neox Cord RT, or Clarix Cord 1K, per square cm
Q4149 **(E/I)**	Excellagen, 0.1 cc
Q4150 **(E/I)**	AlloWrap DS or dry, per square cm
Q4151	Amnioband or Guardian, per square cm
Q4152 **(E/I)**	DermaPure, per square cm
Q4153 **(E/I)**	Dermavest and Plurivest, per square cm
Q4154	Biovance, per square cm
Q4155 **(E/I)**	Neoxflo or Clarixflo, 1 mg

Code	Description
Q4156 **(E/I)**	Neox 100 or Clarix 100, per square cm
Q4157 **(E/I)**	Revitalon, per square cm
Q4158 **(E/I)**	Kerecis Omega3, per square cm
Q4159 **(E/I)**	Affinity, per square cm
Q4160 **(E/I)**	NuShield, per square cm
Q4161 **(E/I)**	Bio-ConneKt wound matrix, per square cm
Q4162 **(E/I)**	WoundEx Flow, BioSkin Flow, 0.5 cc
Q4163 **(E/I)**	WoundEx, BioSkin, per square cm
Q4164 **(E/I)**	Helicoll, per square centimeter
Q4165 **(E/I)**	Keramatrix or Kerasorb, per sq cm
Q4166 **(E/I)**	Cytal, per square centimeter
Q4167 **(E/I)**	TruSkin, per square centimeter
Q4168 **(E/I)**	AmnioBand, 1 mg
Q4169 **(E/I)**	Artacent Wound, per square centimeter
Q4170 **(E/I)**	Cygnus, per sq cm
Q4171 **(E/I)**	Interfyl, 1 mg
Q4173 **(E/I)**	PalinGen or PalinGen Xplus, per square centimeter
Q4174 **(E/I)**	PalinGen or ProMatrX, 0.36 mg per 0.25 cc
Q4175 **(E/I)**	Miroderm, per square centimeter
Q4176 **(E/I)**	Neopatch or Therion, per square centimeter
Q4177 **(E/I)**	FlowerAmnioFlo, 0.1 cc
Q4178 **(E/I)**	FlowerAmnioPatch, per square cm
Q4179 **(E/I)**	FlowerDerm, per square cm
Q4180 **(E/I)**	Revita, per square cm
Q4181 **(E/I)**	Amnio Wound, per square cm
Q4182 **(E/I)**	Transcyte, per square cm
Q4183 **(E/I)**	Surgigraft, per square centimeter
Q4184 **(E/I)**	Cellesta or Cellesta Duo, per sq cm
Q4185 **(E/I)**	Cellesta flowable amnion (25 mg per cc); per 0.5 cc
Q4186	Epifix, per square centimeter
Q4187	Epicord, per square centimeter
Q4188 **(E/I)**	AmnioArmor, per square centimeter
Q4189 **(E/I)**	Artacent AC, 1 mg
Q4190 **(E/I)**	Artacent AC, per square centimeter
Q4191 **(E/I)**	Restorigin, per square centimeter
Q4192 **(E/I)**	Restorigin, 1 cc
Q4193 **(E/I)**	Coll-e-derm, per square centimeter
Q4194 **(E/I)**	Novachor, per square centimeter
Q4195 **(E/I)**	Puraply, per square centimeter
Q4196 **(E/I)**	Puraply AM, per square centimeter
Q4197 **(E/I)**	Puraply XT, per square centimeter

Code	Description
Q4198 **(E/I)**	Genesis amniotic membrane, per square centimeter
Q4199 **(E/I)**	Cygnus matrix, per square centimeter *(effective 01/01/22)*
Q4200 **(E/I)**	SkinTE, per square centimeter
Q4201 **(E/I)**	Matrion, per square centimeter
Q4202 **(E/I)**	Keroxx (2.5g/cc), 1cc
Q4203 **(E/I)**	Derma-Gide, per square centimeter
Q4204 **(E/I)**	Xwrap, per square centimeter
Q4205 **(E/I)**	Membrane Graft or Membrane Wrap, per sq cm
Q4206 **(E/I)**	Fluid flow or fluid gf, 1 cc
Q4208 **(E/I)**	Novafix, per sq cm
Q4209 **(E/I)**	Surgraft, per sq cm
Q4210 **(E/I)**	Axolotl Graft or Axolotl DualGraft, per sq cm
Q4211 **(E/I)**	Amnion bio or axobio sq cm
Q4212 **(E/I)**	Allogen, per cc
Q4213 **(E/I)**	Ascent, 0.5 mg
Q4214 **(E/I)**	Cellesta cord per sq cm
Q4215 **(E/I)**	Axolotl ambient, cryo 0.1 mg
Q4216 **(E/I)**	Artacent cord per sq cm
Q4217 **(E/I)**	WoundFix, BioWound, WoundFix Plus, BioWound Plus, WoundFix Xplus or BioWound Xplus, per sq cm
Q4218 **(E/I)**	SurgiCORD, per sq cm
Q4219 **(E/I)**	SurgiGRAFT-DUAL, per sq cm
Q4220 **(E/I)**	Bellacell HD, Surederm sq cm
Q4221 **(E/I)**	Amniowrap2 per sq cm
Q4222 **(E/I)**	ProgenaMatrix, per sq cm
Q4224 **(E/I)**	Hhf10-p per sq cm
Q4225 **(E/I)**	Amniobind, per sq cm
Q4226 **(E/I)**	MyOwn Skin, includes harvesting and preparation procedures, per sq cm
Q4227 **(E/I)**	Amniocore, per square centimeter *(effective 7/1/20)*
Q4228 **(E/I)**	BioNextPATCH, per square centimeter *(effective 7/1/20)*
Q4229 **(E/I)**	Cogenex Amniotic Membrane, per square centimeter *(effective 7/1/20)*
Q4230 **(E/I)**	Cogenex Flowable Amnion, per 0.5 cc *(effective 7/1/20)*
Q4231 **(E/I)**	Corplex P, per cc *(effective 7/1/20)*
Q4232 **(E/I)**	Corplex, per square centimeter *(effective 7/1/20)*
Q4233 **(E/I)**	SurFactor or NuDyn, per 0.5 cc *(effective 7/1/20)*
Q4234 **(E/I)**	XCellerate, per square centimeter *(effective 7/1/20)*
Q4235 **(E/I)**	AMNIOREPAIR or AltiPly, per square centimeter *(effective 7/1/20)*
Q4236 **(E/I)**	carePATCH, per square centimeter *(effective 7/1/20)*
Q4237 **(E/I)**	Cryo-Cord, per square centimeter *(effective 7/1/20)*
Q4238 **(E/I)**	Derm-Maxx, per square centimeter *(effective 7/1/20)*
Q4239 **(E/I)**	Amnio-Maxx or Amnio-Maxx Lite, per square centimeter. *(effective 7/1/20)*
Q4240 **(E/I)**	Corecyte, for topical use only, per 0.5 cc. *(effective 7/1/20)*
Q4241 **(E/I)**	PolyCyte, for topical use only, per 0.5 cc *(effective 7/1/20)*
Q4242 **(E/I)**	AmnioCyte Plus, per 0.5 cc *(effective 7/1/20)*
Q4244 **(E/I)**	Procenta, per 200 mg *(effective 7/1/20)*
Q4245 **(E/I)**	AmnioText, per cc *(effective 7/1/20)*

Code	Description
Q4246 **(E/I)**	CoreText or ProText, per cc *(effective 7/1/20)*
Q4247 **(E/I)**	Amniotext patch, per square centimeter *(effective 7/1/20)*
Q4248 **(E/I)**	Dermacyte Amniotic Membrane Allograft, per square centimeter *(effective 7/1/20)*
Q4249 **(E/I)**	AMNIPLY, for topical use only, per square centimeter *(effective 10/1/20)*
Q4250 **(E/I)**	AmnioAmp-MP, per square centimeter *(effective 10/1/20)*
Q4251 **(E/I)**	Vim, per square centimeter *(effective 10/1/21)*
Q4252 **(E/I)**	Vendaje, per square centimeter *(effective 10/1/21)*
Q4253 **(E/I)**	Zenith amniotic membrane, per square centimeter *(effective 10/2/21)*
Q4254 **(E/I)**	Novafix DL, per square centimeter *(effective 10/1/20)*
Q4255 **(E/I)**	REGUaRD, for topical use only, per square centimeter *(effective 10/1/20)*
Q4256 **(E/I)**	Mlg complet, per sq cm
Q4257 **(E/I)**	Relese, per sq cm
Q4258 **(E/I)**	Enverse, per sq cm

ICD10 Codes

Code	Description
C07	Malignant neoplasm of parotid gland
C50.011-C50.019	Malignant neoplasm of nipple and areola, female breast (code range)
C50.111-C50.119	Malignant neoplasm of central portion of female breast (code range)
C50.211-C50.219	Malignant neoplasm of upper-inner quadrant of female breast (code range)
C50.221-C50.229	Malignant neoplasm of upper-inner quadrant of male breast (code range)
C50.311-C50.319	Malignant neoplasm of lower-inner quadrant of female breast (code range)
C50.321-C50.329	Malignant neoplasm of lower-inner quadrant of male breast (code range)
C50.411-C50.419	Malignant neoplasm of upper-outer quadrant of female breast (code range)
C50.421-C50.429	Malignant neoplasm of upper-outer quadrant of male breast (code range)
C50.511-C50.519	Malignant neoplasm of lower-outer quadrant of female breast (code range)
C50.521-C50.529	Malignant neoplasm of lower-outer quadrant of male breast (code range)
C50.611-C50.619	Malignant neoplasm of axillary tail of female breast (code range)
C50.621-C50.629	Malignant neoplasm of axillary tail of male breast (code range)
C50.811-C50.819	Malignant neoplasm of overlapping sites of female breast (code range)
C50.821-C50.829	Malignant neoplasm of overlapping sites of male breast (code range)
C50.911-C50.919	Malignant neoplasm of unspecified site of female breast (code range)
C50.921-C50.929	Malignant neoplasm of unspecified site of male breast (code range)
D05.00-D05.92	Carcinoma in situ of breast (code range)
D11.0-D11.9	Benign neoplasm of major salivary gland (code range)
D37.030-D37.039	Neoplasm of uncertain behavior of the salivary glands (code range)
E08.621	Diabetes mellitus due to underlying condition with foot ulcer
E09.621	Drug or chemical induced diabetes mellitus with foot ulcer
E10.621	Type 1 diabetes mellitus with foot ulcer
E11.621	Type 2 diabetes mellitus with foot ulcer
E13.621	Other specified diabetes mellitus with foot ulcer
I83.001-I83.009	Varicose veins of unspecified lower extremity with ulcer (code range)

Code	Description
I83.011-I83.029	Varicose veins of lower extremity with ulcer (code range)
I83.201-I83.229	Varicose veins of lower extremity with both ulcer and inflammation (code range)
I87.311- I87.319	Chronic venous hypertension (idiopathic) with ulcer (code range)
K11.1-K11.9	Disease of salivary gland (code range)
K43.0-K43.2	Incisional hernia (code range)
L97.101-L97.929	Non-pressure chronic ulcer of lower limb, not elsewhere classified (code range)
T20.00XA-T25.399S	Burns - by site and degree of burn (code range)
T30.0	Burn of unspecified body region, unspecified degree
T30.4	Corrosion of unspecified body region, unspecified degree
T31.0-T31.99	Burns (code range)
T32.0-T32.99	Corrosions (code range)
Z85.3	Personal history of malignant neoplasm of breast
Z90.10-Z90.13	Acquired absence of breast and nipple (code range)

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*Key Article

KEY WORDS

Affinity, AlloDerm, AlloMax, AlloSkin, AlloWrap, AmnioBand, Amnioexcel, AmnioMatrix, Apligraf, Artacent Wound, ArthroFlex, Artificial skin, Avaulta Plus, Biobrane, Biobrane l, Bioengineered skin, Biologic tissue, Biovance, Clarix Flo, Collamend, Conexa, Cygnus Solo, Cygnus Matrix, Cygnus Max, Cymetra, Cytal Burn Matrix, Cytal Wound Matrix, DermACELL AWM, DermaMatrix, DermaPure, DermaSpan, Dermavest, Endoform Dermal Template, ENDURAgen, Epicel, EpiCord, EpiFix, Excellagen, E-Z Derm, FlexHD, GammaGraft, Grafix CORE, Grafix PRIME, GraftJacket, GraftJacket Xpress, Graftskin, Guardian, hMatrix, Hyalomatrix, Integra, Integra Bilayer Wound Matrix, Integra Dermal Regeneration Matrix, Integra Flowable Wound Matrix, IntegуPly, Interfyl, Laserskin, MariGen, Mediskin, Miroderm, Neoform, Neox, Neox 1K, Neox Flo, NuShield, OASIS Wound Matrix, OASIS Burn Matrix, OASIS Ultra, Omnigraft, Orcel, Orthoadapt, PalinGen - Membrane, Hydromembrane, Flow, and SportFlow, Pelvicol, Pelvisoft, Permacol, Primatrix, PuraPly, Restore, Revitalon, Skin substitute, StrataGraft, Strattice, SurgiMend, TenSIX, TheraSkin, Tissuemend, TranZgraft, TruSkin, Veritas Collagen Matrix, XCM Biological Tissue Matrix.

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently no Local Coverage Determination (LCD) or National Coverage Determination addressing bioengineered tissue products.
Note: LCD and related articles were retired as of 9/1/16